CLAIMS

1. A DNA fragment having the nucleotide sequence shown in SEQ ID NO: 1 or an analogue or subsequence thereof which

1) has a homology with the DNA sequence shown in SEQ ID NO: 1 of at least 50%, and/or

2) encodes a polypeptide, the amino acid sequence of which is at least 50% homologous with the amino acid sequence shown in SEQ ID NO: 2, and/or

3) encodes a polypeptide which binds an antibody which is also bound by an MSH receptor, and/or

4) encodes a polypeptide which is an MSH receptor or which has the same binding capacity as an MSH receptor.

2. A DNA fragment having the nucleotide sequence shown in SEQ ID NO: 15 or an analogue or subsequence thereof which

1) has a homology with the DNA sequence shown in SEQ ID NO: 15 of at least 50%, and/or

2) encodes a polypeptide, the amino acid sequence of which is at least 50% homologous with the amino acid sequence shown in SEQ ID NO: 16, and/or

3) encodes a polypeptide which binds an antibody which is also bound by an MSH receptor, and/or

4) encodes a polypeptide which is an MSH receptor or which has the same binding capacity as an MSH receptor.

3. A DNA fragment which is a subsequence of the DNA fragment according to claim 1 or 2 which comprises at least 15 nucleo-

tides, preferably at least 18 nucleotides, more preferably at least 21 nucleotides, even more preferably at least 27 nucleotides and most preferably at least 51 nucleotides.

4. A DNA fragment according to claim 1 encoding a polypeptide comprising amino acids no. 1-317 shown in SEQ ID NO: 2.

5. A DNA fragment according to claim 2 encoding a polypeptide comprising amino acids no. 1-325 shown in SEQ ID NO: 16.

6. A DNA fragment which shows at least 55% homology, preferably at least 70%, more preferably at least 80% and most preferably at least 95% homology, to the DNA sequence shown in SEQ ID NO: 1 or SEQ ID NO: 15.

7. A DNA fragment which is a modified DNA fragment or a subsequence thereof which differs from the DNA sequence SEQ ID NO: 1, SEQ ID NO: 15, SEQ ID NO: 5, SEQ ID NO: 7 or SEQ ID NO: 9 or the corresponding subsequence in that at least one nucleotide has been substituted, added, inserted, deleted and/or rearranged.

8. A DNA fragment which is a fusion DNA fragment comprising a DNA fragment according to any of the claims 1-7 in frame with one or more second DNA fragments different from or identical to the DNA fragment according to any of claims 1-7, the second DNA fragment preferably selected from the group consisting of DNA fragments encoding, diphtheria toxin, a staphylococcus protein, a ricin toxin, a pseudomonas endotoxin, abrin and fungal ribosome-inactivation proteins (RIP), the resulting DNA fragment encoding a fusion protein.

9. A DNA fragment having

the nucleotide sequence shown in SEQ ID NO: 3 or an analogue thereof, wherein the nucleotides 13 and/or 15 and/or 23 optionally are substituted by C, or

the nucleotide sequence shown in SEQ ID NO: 4, or an analogue thereof, wherein the nucleotides 19 and/or 29 and/or 32 optionally are substituted by C and wherein the nucleotides 20 and/or 31 optionally are substituted by G.

10. A polypeptide having the amino acid sequence shown in SEQ ID NO: 2 or an analogue or subsequence thereof which

1) is an MSH receptor or is capable of binding to MSH or an analogue thereof, and/or

2) is encoded by a DNA fragment which is at least 50% homologous with the DNA fragment shown in SEQ ID NO: 1, and/or

3) binds an antibody which is also bound by an MSH receptor.

11. A polypeptide having the amino acid sequence shown in SEQ ID NO: 16 or an analogue or subsequence thereof which

1) is an MSH receptor or is capable of binding to MSH or an analogue thereof, and/or

2) is encoded by a DNA fragment which is at least 50% homologous with the DNA fragment shown in SEQ ID NO: 15, and/or

3) binds an antibody which is also bound by an MSH receptor.

12. A polypeptide which is a subsequence of the polypeptide according to claim 10 comprising from 5 to 316 amino acids, preferably at least 7 amino acids, more preferably at least 10 amino acids, even more preferably at least 15 amino acids and most preferably at least 30 amino acids.

13. A polypeptide which is a subsequence of the polypeptide according to claim 11 comprising from 5 to 324 amino acids, preferably at least 7 amino acids, more preferably at least 10 amino acids, even more preferably at least 15 amino acids and most preferably at least 30 amino acids.

14. A polypeptide which shows at least 55% homology, preferably at least 70%, more preferably at least 80% and most preferably at least 95% homology, to the polypeptide shown in SEQ ID NO: 2 or the polypeptide shown in SEQ ID NO: 16.

15. A polypeptide consisting of or comprising

a subsequence of the polypeptide shown in SEQ ID NO: 2, the subsequence being selected from the group consisting of amino acids 1-40, 99-117, 181-189, 268-277, 62-76, 141-158, 212-244, 300-317, 39-63, 75-100, 116-141, 157-182, 188-213, 243-269 and 276-301, and analogues thereof, or

a subsequence of the polypeptide shown in SEQ ID NO: 16 the subsequence being selected from the group consisting of amino acids 1-38, 97-115, 179-187, 265-274, 61-74, 138-156, 211-240, 297-326, 37-62, 73-98, 114-139, 155-180, 186-212, 239-266 and 273-298, and analogues thereof.

16. A polypeptide according to any of claims 10-15 which is glycosylated and/or coupled to a carbohydrate or lipid moiety and/or contains a palmitoyl anchor or a part thereof and/or provided with a detectable label and/or coupled to a solid support.

17. A polypeptide which is a fusion polypeptide comprising a polypeptide according to any of claims 10-16 or a subsequence thereof fused to a second polypeptide which may be different from or identical to the polypeptide according to any of

claims 10-16, which fusion polypeptide preferably has retained the capability of binding to MSH or an analogue thereof.

18. A polypeptide according to any of claims 10-17 in substantially pure form.

19. A polypeptide according to any of claims 10-18 in lipid soluble form.

20. A DNA fragment or a subsequence or analogue thereof which

shows a homology with any of the nucleotide sequences shown in SEQ ID NO: 5, SEQ ID NO: 7 or SEQ ID NO: 9 of at least 40%, preferably 50%, more preferably at least 55%, even more preferably at least 70%, still more preferably at least 80% and most preferably at least 95%, and/or

which can be isolated by using the nucleotide sequence shown in SEQ ID NO: 13 and/or SEQ ID NO: 14 as a primer, and/or

which has the nucleotide sequence shown in SEQ ID NO: 5, SEQ ID NO: 7 or SEQ ID NO: 9.

21. A DNA fragment which is a fusion DNA fragment comprising a DNA fragment according to claim 20 in frame with one or more second DNA fragments different from or identical to the DNA fragment according to claim 20, the second DNA fragment preferably being selected from the group consisting of DNA fragments encoding a melanotropic hormone receptor, an MSH receptor and an ACTH receptor.

22. A polypeptide or a subsequence or analogue thereof, which shows a homology of at least 40%, preferably at least 50%, more preferably at least 55%, even more preferably at least 70%, still more preferably at least 80% and most preferably

at least 95% with the polypeptide shown in SEQ ID NO: 6, SEQ ID NO: 8 or SEQ ID NO: 10.

23. A polypeptide which is a fusion polypeptide comprising a polypeptide according to claim 22 or a subsequence thereof fused to a second polypeptide which may be different from or identical to the polypeptide according to claim 22, the second polypeptide preferably being selected from the group consisting of a melanotropic hormone receptor, an MSH receptor and an ACTH receptor or an analogue or subsequence thereof.

24. A DNA fragment coding for a polypeptide as defined in any of claims 10-19, 22 and 23.

25. A replicable expression vector carrying a DNA fragment according to any of claims 1-9, 20, 21 and 24, which vector is capable of replicating in a host organism or a cell line.

26. A vector according to claim 25 which is

pB-11D deposited under the deposition number DSM 7214 at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH, or

pE-MC-2 deposited under the deposition number DSM 8440 at Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH.

27. A cell which carries and is capable of replicating the DNA fragment according to any of the claims 1-9, 20, 21 and 24.

28. A cell according to claim 27, which is selected from the group consisting of a bacterium, a yeast and a protozoan, or the cell is derived from a multicellular organism selected from the group consisting of a fungus, an insect, a plant, and a mammal, and the cell preferably being a bacterium

selected from the group consisting of the genus *Bacillus*, *Escherichia* and *Salmonella*.

29. A method of producing a polypeptide as defined in any of claims 10-19, 22 and 23, comprising the following steps of:

(a) inserting a DNA fragment as defined in any of the claims 1-9, 20, 21 and 24 into an expression vector,

(b) transforming a suitable host cell according to claim 27 or 28 with the vector produced in step (a),

(c) cultivating the host cell produced in step (b) under suitable conditions for expressing the polypeptide,

(d) harvesting the polypeptide, and

(e) optionally subjecting the polypeptide to posttranslational modification,

or comprising liquid and/or solid phase peptide synthesis procedures.

30. A stable cell line which produces the polypeptide according to claim 10 or 11 and which preferably contains and expresses cDNA encoding the polypeptide of claim 10 or claim 11.

31. A method of preventing or stimulating the coupling of an MSH receptor to its guanine nucleotide binding protein in an animal, in particular a mammal, comprising administering a substance which in advance has been found to bind to a polypeptide according to any of claims 10-19 so as to occupy one or several of the cytoplasmic loops and/or the C-terminal sequence.

32. A method of preventing or stimulating the binding of MSH and similar peptides to an MSH receptor in an animal, in particular a human, comprising administering, to the animal, a substance which in advance has been found to bind to a polypeptide according to any of claims 10-19 so as to occupy the binding site of the receptor using an antagonist, a blocker or a compound such as a derivative of MSH having a structure similar to MSH, and optionally thereby preventing or stimulating the generation of second messenger elements.

33. A method of increasing or decreasing the generation of second messenger elements, and/or increasing or decreasing the production of an MSH receptor and/or optionally increasing or decreasing the binding affinity of MSH to an MSH receptor, comprising administering to an animal, in particular a human, a medicament which is or becomes bound to a substance which in advance has been found to bind to a polypeptide according to any of claims 10-19.

34. A method of targeting, with a medicament, a cell that contains an MSH receptor on its surface, comprising administering a substance optionally linked to a medicament which substance in advance has been found to bind to a polypeptide according to any of claims 10-19 and which substance binds to the MSH receptor.

35. A method according to the claim 34 wherein the medicament is a radionuclide or a toxin or any other molecule of natural or synthetic origin.

36. A method according to any of claims 31-35 for the treatment of an MSH receptor expressing disease condition selected from the group consisting of melanoma, skin cancer, vitiligo, pyretic condition, inflammatory condition, nociceptive condition, catatonic condition, impaired memory condition, reduced or increased skin tanning, pigmentation condition, epilepsy and nerve damage.

37. A method for treating conditions caused by MSH receptor deficiency or impaired MSH receptor function in a mammal, such as a human, comprising administering a polypeptide according to claim 19 which is an MSH receptor, or is capable of binding to MSH, or is an analogue thereof, to the mammal.

38. A method for treating conditions caused by MSH receptor deficiency or impaired MSH receptor function, such as tyrosinase-positive albinism, in a mammal, such as a human, comprising introducing a DNA fragment according to any of claims 1-9, 20, 21 and 24 encoding an active form of an MSH receptor.

39. A method for increasing or decreasing the melanin content of the skin in a mammal, such as a human, comprising administering substances as defined in any of claims 31-34 that are active through an MSH receptor, preferably to increase the skin tanning without or with reduced exposure to sunlight or to avoid sunburns.

40. A method of activating the antipyretic and/or anti-inflammatory and/or antinociceptive and/or memory improving and/or nerve regenerating action effected via an MSH receptor, comprising administering a substance that acts on the MSH receptor to bring about the antipyretic and/or anti-inflammatory and/or antinociceptive and/or memory improving and/or nerve regenerating actions.

41. A method of diagnosing an MSH receptor expressing disease condition such as melanoma or skin cancer, comprising targeting a cell containing an MSH receptor on its surface with diagnostic agent capable of binding to the MSH receptor, which diagnostic agent can be detected following binding to the receptor.

42. The method according to claim 41, as used in the assessment of the prognosis and/or guidance for further treatment of melanoma or skin cancer.

43. A method for detecting an MSH receptor in a biological sample, such as a tissue sample, a cell culture or a cell suspension, wherein the sample is treated with a optionally labelled substance that binds to the MSH receptor, and detecting or visualizing the presence of the bound substance.

44. An antibody optionally provided with a detectable label which antibody is reactive with a polypeptide according to any of claims 10-19, 22 and 23 and which is preferably a monoclonal antibody.

45. A method for detection and/or quantitation of the MSH receptor mRNA, comprising extracting RNA from a biological sample such as a cell, a tissue sample, a cell culture or a cell suspension and measuring the hybridization of said RNA to a labelled DNA fragment according to any of claims 1-9, 20, 21 and 24 or a labelled RNA fragment constructed from the DNA fragment according to any of claims 1-9, 20, 21 and 24.

46. A method for detection and/or quantitation of the MSH receptor mRNA, comprising extracting RNA from cells or tissues and converting it into cDNA for subsequent use in the polymerase chain reaction (PCR), preferably using PCR primer(s) which is/are synthesized based on the DNA fragment claimed in any of claims 1-9, 20, 21 and 24.

47. The use of any of the methods of claims 43, 45 and 46 for diagnosis of an MSH receptor expressing disease condition such as melanoma and skin cancer.

48. The use of a DNA fragment according to any of claims 1-9, 20, 21 and 24 for the isolation of other similar DNA fragments using techniques such as PCR or hybridization.

49. The use of a polypeptide according to any of claims 10-19, 22 and 23 for designing DNA probes for use in techniques such as PCR and hybridization.

50. The use of a polypeptide according to any of claims 10-19, 22 and 23 for the deduction of the three-dimensional structure of an MSH receptor or an analogue thereof having MSH binding capacity for use in the design of a substance capable of binding to the MSH receptor.

51. A method for selecting a substance which is capable of binding to a melanotropic hormone receptor polypeptide such as an MSH receptor and which substance may optionally be capable of preventing or stimulating the generation of a second messenger element in a cell such as a mammalian cell, in particular a human cell, by its binding to the melanotropic hormone receptor polypeptide the method comprising one or more of the following steps:

1a) incubating a sample containing a melanotropic hormone receptor polypeptide or an analogue thereof, the melanotropic hormone receptor polypeptide preferably being a polypeptide according to any of claims 10-19, 22 and 23, with radioactively labelled melanotropic hormone or an analogue thereof and with the substance to be tested, and

1b) measuring the binding affinity of the substance to be tested for the melanotropic hormone receptor polypeptide by separating bound from free labelled melanotropic hormone or an analogue thereof using either filtration, centrifugation, superflow or chromatography followed by measuring the radioactivity retained in the sample by standard nuclear counting,

or

2a) incubating a sample containing a melanotropic hormone receptor polypeptide or an analogue thereof, the melanotropic hormone receptor polypeptide preferably being a polypeptide according to any of

claims 10-19, 22 and 23, with melanotropic hormone or an analogue thereof and with the substance to be tested, and

2b) measuring the binding affinity of the substance to be tested for the melanotropic hormone receptor polypeptide by separating free melanotropic hormone or the analogue thereof from the bound melanotropic hormone or the analogue thereof using either filtration, centrifugation, superflow or chromatography followed by measuring the bound melanotropic hormone or the analogue thereof by a detection system capable of detecting melanotropic hormone or the analogue thereof, preferably using a detection system such as radio immunoassay, immunefluorescense assay, UV light absorption spectrometry or fluorescence emission spectrometry.

52. A method for selecting a substance which is capable of binding to a melanotropic hormone receptor polypeptide such as an MSH receptor and which substance may optionally be capable of preventing or stimulating the generation of a second messenger element in a cell such as a mammalian cell, in particular a human cell, by its binding to the melanotropic hormone receptor polypeptide the method comprising one or more of the following steps:

1a) incubating a sample containing a melanotropic hormone receptor polypeptide or an analogue thereof linked to a solid support, the melanotropic hormone receptor polypeptide preferably being a polypeptide according to any of claims 10-19, 22 and 23, with melanotropic hormone or an analogue thereof and with the substance to be tested, and

1b) measuring the binding affinity of the substance to be tested for the melanotropic hormone receptor polypeptide or an analogue thereof by separating

free melanotropic hormone or an analogue thereof from the melanotropic hormone or an analogue thereof bound to the melanotropic hormone receptor polypeptide or analogue thereof by washing, followed by measuring the bound melanotropic hormone or an analogue thereof by using a ligand, preferably an antibody, capable of binding to the bound melanotropic hormone or an analogue thereof which ligand is in itself detectable, or which ligand is a first ligand which can be rendered detectable using a second ligand, preferably an antibody capable of binding to the said first ligand,

or

2a) incubating a sample containing, preferably in a soluble form or in a solid phase being attached to a matrix, the melanotropic hormone receptor polypeptide which preferably is a polypeptide according to any of claims 10-19, 22 and 23 or an analogue thereof, with melanotropic hormone and with the substance to be tested, and

2b) measuring the alteration in the degree of interaction of the melanotropic hormone receptor with a G-protein caused by the binding of the substance to be tested to the melanotropic hormone receptor.

53. A method according to any of claims 31-34, 39, 40, 43, and 50-52 wherein the substance is an antibody or a part thereof or a molecule of natural or synthetic origin having affinity for an MSH receptor or the melanotropic hormone receptor polypeptide.